

Engineering Viruses for Health or Warfare

The Washington Post

SUNDAY, AUGUST 16, 1970

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A Nobel Prize winner, Lederberg is professor of genetics at the Stanford University School of Medicine. The following article includes remarks he made at a recent informal session of the disarmament conference committee at Geneva, which is considering proposals for the elimination of biological and chemical weapons.

RECENT ADVANCES in molecular biology have important implications for human welfare. On the one hand, they help man to a deeper understanding of his own evolution and functioning as the most complex of life forms on earth. They support revolutionary advances in medicine in such fields as cancer, aging, congenital disease and virus infections. They will also play a vital role in agriculture and related industries.

On the other hand, molecular biology might be exploited for military purposes and result in a biological weapons race whose aim could well become the most efficient means for removing man from the planet. For example, Prof. Gobind Khorana of the University of Wisconsin recently reported the synthetic assembly of a small gene through chemical operations on DNA components. It will be a major step to extend this technical capability to the synthesis of small viruses.

But this surely could be accomplished within the next decade. This procedure will allow an unlimited range of experimental variations of the genetic structure of different viruses, a process that has many important potential applications for human health. It also offers us the prospect of engineering the design of viruses to exquisite detail, for vaccines or for weapons. Accomplishments like Khorana's have been possible in a small laboratory on an annual research budget that is minuscule compared to weapons hardware. A serious military investment in this area could be expected to outstrip this already breathtaking pace of advance by many fold.

Threat to Man

FOR MANY YEARS biological warfare has been given only incidental attention as a subject of diplomatic discussion, for it seemed to have little bearing on the adjustments of power that were the main work of specialists in foreign affairs.

We now begin to realize that the intentional release of an infectious particle, be it a virus or bacterium, from the confines of the laboratory or of medical practice must be formally condemned as an irresponsible threat against the whole human community.

A large epidemic, involving millions of people spread over time and space, is an immensely complicated phenomenon about which it is very difficult to make accurate scientific predictions. This combination of very grave potential hazard with a high degree of unpredictability is a peculiar attribute of biological weaponry at its present stage of development. This has a great deal to do with the rational doctrine that so far has placed a relatively low value on its military utility.

It Could Be Too Late

THE PRESENT situation thus might provide the most favorable opportunity for international action to regulate the further development and proliferation of biological warfare. I am convinced we know enough about it to have legitimate concern about its future prospects. Until now no nation appears to have staked its security to any significant degree on BW armaments. I would therefore hope this provides a basis for accord. If we wait until BW has been developed into a reliable armament for use under a range of military doctrine, we must all fear that it could then be too late to disengage important powers from their commitment to it.

The barriers that now give advanced countries a measure of protection against plague could be breached by further technical developments if a substantial effort were to be applied during the next decade to making the plague bacillus into a weapon.

Other infectious agents might be even more adaptable. Some of man's deadliest enemies are viruses which, like yellow fever, are transmitted by mosquitos or other arthropods. These have the advantage, from a military standpoint, that they should not start a potentially retroactive epidemic in areas where the vector insect does not normally abound. It is already evident that such insect-borne viruses could be applied in the first instance by direct aerial dissemination, with little or no further spread from the first wave of infected targets.

Recent reports of airborne or pneumonic rabies, a terrible disease, which is normally spread by the bite of an infected dog or other animal, illustrate this possibility. There is then the danger that, if a large nucleus of people is attacked in this way, further evolution of the virus will occur to give rise to a new form of the disease that does spread from person to person, contrary to the calculations of the attacker. The Black Death itself underwent a similar evolution from the original bubonic flea-borne plague to outbreaks of the far more contagious pneumonic variety.

We have learned in recent years that viruses undergo constant evolution in their own natural history, not only by mutations within a given strain, but also by the natural cross-hybridization of viruses that superficially appear to be only remotely related to one another. Furthermore, many of us already carry viruses in our body cells of which we are unaware for years, and which may be harmless—though they may eventually cause the formation of a tumor, or of brain degeneration or other diseases. At least in the laboratory, we can show that such latent viruses can still cross-breed with other viruses to give rise to many new forms.

My gravest concern is that similar scientific breakthroughs of a rather predictable kind will be made and their potential military significance exploited, so as to result in a transformation of current doctrine about "unreliable" biological weapons. We are all familiar with the process of mutual escalation in which the defensive efforts of one side inevitably contribute to further technical developments on the other and vice versa. The mere existence of such a contest produces a mutual stimulation of effort; moreover, there is no practical system of counterintelligence that will protect secret work for an indefinite period of time from becoming known to others. And the potential undoubtedly exists for the design and development of infective agents against which no credible defense is possible, through the genetic and chemical manipulation of these agents.

Subversion of Science

PERMIT ME, now, to ask a rhetorical question: Can we establish a world order that will, in effect, protect "you," as representatives of the global community, from the subversion of the scientific advances to which my own peers and myself have dedicated their careers?

I wish I could be sure that such a remark would always be received with an understanding of the ironic spirit with which it is uttered. I do not have to tell you of the worldwide attack on science, the flight from reason that has tempted so many young people and makes so many dilemmas for those of us in university life.

What the youth see as the perversion of knowledge is, I believe, an important aspect of their repudiation of us. Among the undergraduates at my own university, there is no prospect more disheartening than the idea that even health research is subject to exploitation in the most inhumane direction imaginable.

For many years I have advocated that the control of biological warfare be given a special place in international and national initiatives for reasons I have mentioned. I am deeply gratified that President Nixon's announcement (last Nov. 25), which disavowed offensive biological warfare development, has made it possible for me to address these issues in terms fully consistent with the policy of the government of my own country.

Even after agreement to eliminate biological weapons, we will still remain very vulnerable to a form of biological warfare that is beyond the reach of any covenant that we can make. This is the warfare practiced upon us by nature, the unremitting barrage of infection by old and by new agents that still constitute a very large part of the perils to normal and healthy life.

Vexing Virus Infections

WE HAVE ALL had vexing, perhaps even tragic, personal experiences with virus infections. You will all recall the global epidemic of influenza that was first identified in Hong Kong about three years ago. This was not a particularly severe form of the virus and its eventual mortality was probably only in the tens of thousands.

You will also recall having read from time to time about small outbreaks of mysterious new diseases like "Lassa fever" and the "Marburg virus." These were both extremely dangerous threats; and while much credit must be given to the diligence of the medical people who dealt with the outbreaks, a large element of pure luck was involved in localizing these incidents. We must expect that there are many additional viruses already indigenous to primate and human populations in primitive areas and to which the inhabitants of advanced countries are extremely vulnerable.

Yellow fever is a historically important disease that now belongs in the same category. It is now maintained on earth mainly through an animal reservoir of infection, in the monkeys in tropical jungles. Urban populations are now protected from yellow fever by campaigns to abolish the fever-carrying species of mosquitos in South America and by the availability of excellent vaccines in advanced countries. Mosquito species capable of transmitting yellow fever are, however, abundant in South Asia and the accidental introduction of yellow fever, for example, into India would be a human tragedy of catastrophic dimensions. Specialists in epidemiology are quite puzzled

that this accident has not already happened and we have no good explanation for this good fortune.

My purpose is not to suggest the vulnerability of the Asian continent to biological military attack but rather to point out immense gaps in the pattern of international cooperative defenses that should be mounted but which have a relatively feeble standing in the present-day world.

Threat to Crops

COUNTRIES THAT are undergoing a transition in the development of their agriculture are vulnerable to analogous threats in biological warfare directed against crops as distinguished from human targets. These are now newly vulnerable to destruction by plant pests of either natural or artificial origin. An outbreak of "coffee rust" is at this moment a serious threat to the agriculture and economy of Brazil; hoof-and-mouth disease made a costly incursion into British cattle a few years ago.

The promulgation of an international agreement to control biological warfare in a negative sense should, therefore, be accompanied by steps urgently needed to build positive efforts at international cooperation, a kind of defensive biological research against natural enemies of the human species.

One of the best assurances that any country might have that the microbiological research of its neighbors was directed toward human purposes would be constantly expanding participation in international health programs. Any country that publicly and avowedly subscribed to the total renunciation of secret BW research might conceivably be able to continue clandestine efforts without revealing their substantial content. It would, however, have great difficulty in maintaining such an effort, at any substantial level or quality of operation, while still keeping its very existence secret. Therefore, besides the obvious direct health benefits of expanded international cooperation we would also be rewarded by a higher level of mutual assurance that every party was indeed living up to the spirit of its obligations under a BW convention.

In conclusion, let me say that some of the speculations I have mentioned are ones that all of us must fervently hope will never materialize. But it would seem to me both foolish and arrogant to assume that our goodwill alone, without concrete arrangements, will serve to forestall the further development, proliferation and possible eventual recourse to what surely is one of the most ghastly methods of warfare imaginable.